



## Primary pulmonary carcinoid tumor with metastasis to endometrial polyp

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### ABSTRACT

**INTRODUCTION:** A carcinoid tumor occurring in the endometrium has been documented in the literature, but there is no report in regard to carcinoid tumor metastasis to endometrium.

**PRESENTATION OF CASE:** We report a case of a malignant carcinoid metastasis to an endometrial polyp. Patient underwent hysteroscopy, and polypectomy. The pathology demonstrated an endometrial polyp containing a 4 mm x 5 mm nodule of metastatic carcinoid tumor, consistent with metastasis from patient's known pulmonary carcinoid. The tumor was morphologically similar to the tumors of the right lung, with similar immune-profile.

**DISCUSSION:** This patient presented with a suspicious pelvic ultrasound. Due to her age, the first priority was to exclude uterine cancer. The endometrial polyp, which was found, had a small focus of metastatic carcinoid tumor. To the best of our knowledge, this finding has not been previously recorded in the literature. Our patient also had a history of metastatic carcinoid tumor to breast. This finding is also very uncommon.

**CONCLUSION:** This is the first case in the literature described a malignant carcinoid metastasis to an endometrial polyp.

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### 1. Introduction

We report a case of a malignant carcinoid metastasis to an endometrial polyp which to the best of our knowledge has not been previously recorded in the literature. Carcinoid tumors were first described over 100 years ago by Lubarsch, who found multiple tumors in the distal ileum of two patients at autopsy.<sup>1</sup> Oberndorfer used the term *karzinoide* in 1907 to describe similar tumors that appeared to behave in a more indolent fashion than typical adenocarcinomas.<sup>2</sup> A carcinoid tumor occurring in the endometrium has been documented in the literature,<sup>3,4</sup> but there is no report in regard to carcinoid tumor metastasis to endometrium. This patient also had mammary manifestation of metastatic carcinoid tumor, which is extremely rare.<sup>5</sup>

### 2. Case report

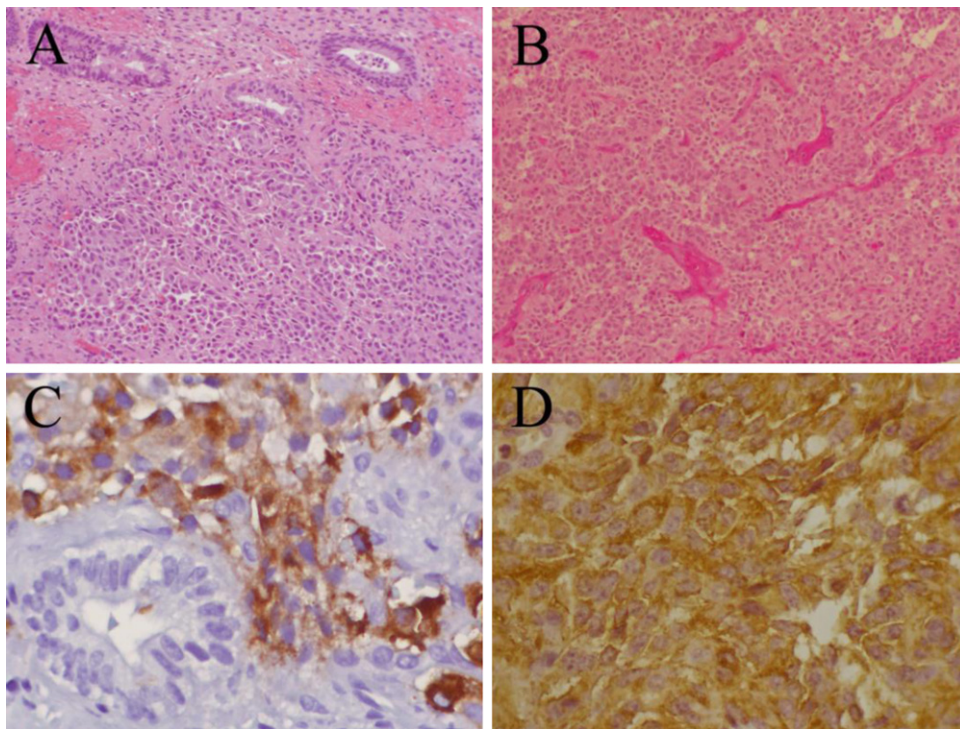
The patient gave her informed consent in order for her case to be presented. A 70-year-old white post menopausal woman with history of carcinoid tumor of the lung was referred to the gynecologic

oncology service after pelvic transvaginal sonography revealed an abnormal thickening of the endometrial echo complex measuring up to 1.4 cm at the uterine fundus. The finding was suggestive of an interval enlargement of a known polyp. The patient had experienced no postmenopausal uterine bleeding. Confirmatory sonohystogram revealed a cystic polyp at the fundus of the uterus measuring 15 mm x 13 mm. Patient underwent hysteroscopy and polypectomy without complication. The final pathology revealed the endometrial polyp to encompass a nodule of metastatic carcinoid.

The history of present illness began in October 1993 when a chest X-ray was notable for a right lung nodule. The patient underwent right thoracotomy with right lower lobectomy. Three tumors were found. All were pathological carcinoid. In 2005 (12 years later), she underwent left thoracotomy with resection of the left lower lobe. A 2.2 cm carcinoid tumor and multiple additional carcinoid tumorlets measuring up to 0.4 cm were removed. In 2008 the patient underwent an ultrasound guided core biopsy of a left breast lesion. Pathology again revealed metastatic carcinoid with similar histologically to the patient's initial lung carcinoid. The patient was initiated on Octreotide therapy. Which she currently receives on a monthly basis. Additional medical history is notable for severe asthma, gastroesophageal reflux disease, recurrent bronchiectasis, recurrent bronchitis, and recurrent pneumonia. The patient's family history is significant for colorectal cancer in her father, and no breast or gynecologic cancer in her family.

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**Fig. 1.** Endometrial metastatic carcinoid tumor and primary right lung tumor. Both tumors exhibit strong chromogranin positivity: (A) endometrium H&E 100 $\times$ ; (B) primary lung tumor H&E 100 $\times$ ; (C) endometrium chromogranin 400 $\times$ ; and (D) primary lung tumor chromogranin 400 $\times$ .

### 3. Surgical pathology

Pathology demonstrated an endometrial polyp containing a 4 mm  $\times$  5 mm nodule of metastatic carcinoid tumor, consistent with metastasis from patient's known pulmonary carcinoid. Immunohistochemical studies show that the specimen was strongly positive for chromogranin and synaptophysin. It was negative for Cytokeratin AE1/AE3 and equivocal for thyroid transcription factor 1 (TTF1). The tumor was morphologically similar to the tumors of the right lung in 1993, with similar immune-profile (Fig. 1). The specimens from the carcinoid tumor from the left lung obtained by fine needle biopsy in 2005, and the right breast in 2008 were similar morphologically to that in the endometrial polyp. Both were positive for chromogranin and synaptophysin, but they were also positive for Cytokeratin AE1/AE3 and TTF1.

### 4. Discussion

This patient presented with a suspicious pelvic ultrasound. Due to her age, the first priority was to exclude uterine cancer. The patient underwent hysteroscopic resection and endometrial sampling. The endometrial polyp had a small focus of metastatic carcinoid tumor. To the best of our knowledge, this finding has not been previously recorded in the literature. Our patient also had a history of metastatic carcinoid tumor to breast. This finding is also very uncommon. A review of the literature by Fishman et al. disclosed only 13 reported cases of carcinoid tumor metastatic to the breast.<sup>5</sup>

Carcinoid (typical carcinoid and atypical carcinoid) tumor is a well differentiated neoplasm and part of the neuroendocrine tumor family; well and poorly differentiated neuroendocrine tumors are grouped together only because of generic neuroendocrine marker expression such as synaptophysin and chromogranin. These tumors are thought to arise from the neuroendocrine tissue of the aerodigestive, gynecologic, and genitourinary tracts.<sup>6</sup>

Carcinoid tumor can originate from fore-gut, mid-gut and hind-gut. Fore-gut carcinoid tumors most commonly originate in the lungs, bronchi, or stomach; mid-gut carcinoid tumors most commonly originate in the small intestine, appendix, and proximal large bowel; and hind-gut carcinoid tumors originate in the distal colon and rectum. The overall incidence of carcinoid tumors in the United States is estimated to be 5–6 cases per 100,000 people.<sup>7</sup> Yao et al. noted a significant increase in reported annual age-adjusted incidence from 1973 (1.09/100,000) to 2004 (5.25/100,000).<sup>7,8</sup> Because many carcinoid tumors are indolent, their true incidence may be higher. A Swedish study reviewed both surgical specimens and autopsies in a single geographic location and reported the incidence to be 8.4 cases per 100,000 people.<sup>9</sup> An analysis of 35,825 cases by Yao et al. in the United States showed the locations of the primary tumors varied significantly by sex. Female patients were more likely to have a primary tumor in the lung, stomach, appendix, or cecum, whereas male patients were more likely to have a primary tumor in the thymus, duodenum, pancreas, jejunum/ileum, or rectum. The primary tumor sites also varied significantly by race. In particular, the lung was the primary site more often among Caucasian patients (30%) than among patients in the other racial groups.<sup>7</sup>

Pulmonary carcinoid makes up approximately 2% of primary lung tumors.<sup>10,11</sup> They are thought to arise from neuroendocrine Kulchitsky's cells located in the bronchial mucosa.<sup>12,13</sup> The majority of the tumors are peri-hilar in location, and patients often present with recurrent pneumonia, cough, hemoptysis, or chest pain.<sup>14</sup> Lung carcinoids may secrete various hormones, giving rise to a carcinoid syndrome, a variant carcinoid syndrome or rarely Cushing's syndrome, acromegaly, or other peptide produced endocrine syndrome.<sup>15</sup> Well-differentiated pulmonary neuroendocrine tumors are usually indolent, with metastases reported in less than 15% of cases.<sup>14,16,17</sup> When they do occur, metastases usually can develop in mediastinal lymph nodes, liver, bone, skin, or brain. This patient developed metastasis to her breast. It is likely that this patient's multiple pulmonary carcinoids associated with

multiple tumorlets were not metastasis but rather metachromic primary carcinoid arising from a background of “Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia” (DIPNECH).<sup>18</sup>

In the gynecological Oncology literatures, it is well recognized that carcinoid tumors can arise within ovarian teratomas.<sup>19–21</sup> Rare cases have been described in the uterine cervix.<sup>22</sup> A carcinoid tumor of the endometrium has been described by Albores-Saavedra et al. and extension from such an origin into the myometrium would account for the intramuscular location of this tumor; and this tumor histologically was similar to the mid-gut carcinoid<sup>4</sup>; there is no obvious embryological link to explain this finding. Primary carcinoid tumors of the ovary account for less than 0.1% of all ovarian neoplasms.<sup>6</sup> These tumors are typically classified as germ cell tumors of the ovary and can be divided into four categories: Insular, Trabecular, Mucinous and Strumal.<sup>6,23</sup> The insular and trabecular are the most common subtypes that metastasized to the ovary. Given the rarity of the disease, it is also critical to rule out a metastatic GI primary that could metastasize to the ovary, and tends to present as bilateral ovarian metastases.<sup>6</sup> Microscopically, the metastatic carcinoid is composed of tumor nodules, whereas primary ovarian carcinoid forms a single homogenous mass. The presence of other teratomatous elements that are associated with an ovarian carcinoid confirms that it is of primary ovarian origin. In our case the immune-profile of carcinoid nodule of endometrial polyp was consistent with metastasis from patient's known pulmonary carcinoid.

#### Conflict of interest statement

None.

#### Funding

None.

#### Consent

We obtained written and signed consent to publish the case report from the patient.

#### Author contributions

Mazdak Momeni, M.D.; Howard H. Mizrachi, M.D. – manuscript writing, editing, and picture preparation.

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